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Propofol–alfentanil *vs* propofol–remifentanil for posterior spinal fusion including wake-up test

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Background. Wake-up test can be used during posterior spinal fusion (PSF) to ensure that spinal function remains intact. This study aims at assessing the characteristics of the wake-up test during propofol–alfentanil (PA) *vs* propofol–remifentanil (PR) infusions for PSF surgery.

Methods. Sixty patients with scoliosis and candidates for PSF surgery were randomly allocated in either alfentanil (PA) or remifentanil (PR) group. After an i.v. bolus of alfentanil 30 $\mu g\ kg^{-1}$ in the PA group or remifentanil 1 $\mu g\ kg^{-1}$ in the PR group, anaesthesia was induced with thiopental and atracurium. During maintenance, opioid infusion consisted of alfentanil 1 $\mu g\ kg^{-1}\ min^{-1}$ or remifentanil 0.2 $\mu g\ kg^{-1}\ min^{-1}$, in the PA group and the PR group, respectively. All patients received propofol 50 $\mu g\ kg^{-1}\ min^{-1}$. Atracurium was given to maintain the required surgical relaxation. At the surgeon's request, all infusions were discontinued. Patients were asked to move their hands and feet. Time from anaesthetic discontinuation to spontaneous ventilation (T_1), and from then until movement of the hands and feet (T_2), and its quality were recorded.

Results. The average T_1 and T_2 were significantly shorter in the PR group [3.6 (2.5) and 4.1 (2) min] than the PA group [6.1 (4) and 7.5 (4.5) min]. Quality of wake-up test, however, did not show significant difference between the two groups studied.

Conclusion. Wake-up test can be conducted faster with remifentanil compared with alfentanil infusion during PSF surgery.

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Spinal cord injury, which may occur as a result of vascular compromise by mechanical deformation, is one of the most dangerous but rare complications after operative correction of scoliosis.[1 2] Incidence of acute neurological complications during posterior spinal fusion (PSF), vary between 0.7 and 5%.[2–4] Intra-operative monitoring of the spinal cord function during PSF has been recommended to avoid permanent neurological damage.[5–8] Intra-operative wake-up test is used to analyse the integrity of the spinal motor function.[8 9]

Total i.v. anaesthesia (TIVA) with propofol and opioids has a favourite pharmacokinetic profile attributable to its short-action and rapid recovery.[8] Although, alfentanil has been frequently used during TIVA,[10 11] its dose for prolonged infusion has been limited because of the accumulation and risk of prolonged recovery.[12] Remifentanil is an opioid with an extremely rapid clearance and an ultra-short half-life.[13] This pharmacological profile of remifentanil may be useful for spinal procedures, where rapid recovery, immediate neurological examination and haemodynamic stability are desirable.[14]

Therefore, we decided to compare speed and quality of the intra-operative wake-up test during either propofol–alfentanil (PA) or propofol–remifentanil (PR) TIVA.

Methods

After approval of the Ethics' Committee and having obtained written informed consent, 60 patients of both sexes with idiopathic scoliosis, aged 14–28 yr, ASA physical status II, undergoing elective posterior thoracolumbar spinal fusion (PSF) with either Diapason or Cotrel–Dubousset

rods instrumentation were enrolled in this prospective and randomized study. They were randomly allocated to receive either PA or PR infusion according to a table of random number. Patients with severe cardiovascular, pulmonary, renal, hepatic, and psychiatric diseases, epilepsy, impaired verbal contact, inability in moving feet, diseases affecting muscle function, chronic exposure to opioids, or having known hypersensitivity to propofol, and pregnant women were excluded.

All enrolled patients received detailed instructions about the wake-up test the day before surgery. They did not receive any sedative premedication before the day of surgery. On arrival in the operating room at the morning of surgery, an 18 gauge i.v. catheter was inserted, and Ringer solution was administered at a rate of 7 ml kg^{-1} h^{-1} for replacement of volume deficit before the induction of anaesthesia. All patients' vital signs (ECG and heart rate, oxygen saturation, non-invasive blood pressure) were continuously monitored throughout the operation and until discharge from recovery room.

All patients were preoxygenated for 3 min. After i.v. administration of midazolam 30 μg kg^{-1} in both groups, alfentanil (30 μg kg^{-1}) in PA group or remifentanil (1 μg kg^{-1}) in PR group were injected i.v. 2 min before induction of anaesthesia. Thereafter, anaesthesia was induced with thiopental 5 mg kg^{-1} and atracurium 0.6 mg kg^{-1}. Two minutes later, the trachea was intubated with a cuffed oro–endotracheal tube, and the lungs were mechanically ventilated, using tidal volumes of 8–10 ml kg^{-1} at a rate of 10–12 min^{-1} (Sulla 808, PM 8040, Dräger Medical, Lübeck, Germany), to maintain end tidal CO_2 between 4 and 4.5 kPa. Bladder catheter, arterial cannula and two additional 18 gauge venous catheters were inserted. Thereafter, patients were moved to the prone position and prepared for surgery.

Anaesthesia was maintained with a continuous infusion of propofol 50 μg kg^{-1} min^{-1} and alfentanil (1 μg $kg^{-1}min^{-1}$) or remifentanil (0.2 μg kg^{-1} min^{-1}) in the PA or PR group, respectively. If systolic arterial pressure decreased below 80 mm Hg or if bradycardia (defined as a heart rate less than 50 beats min^{-1}) occurred, all infusions were reduced by 50%. A second injection of atracurium 0.2 mg kg^{-1} was given upon the skin incision to facilitate surgical exposure. Supplemental doses of atracurium 0.2 mg kg^{-1} were thereafter administered every 20 min if needed, based on neuromuscular monitoring.

Patients were kept mildly hypotensive (systolic arterial pressure under 100 mm Hg or to a level of up to 30% of preinduction baseline), by i.v. administration of hydralazine 100 μg kg^{-1}, repeated every 15 min up to a total dose of 300 μg kg^{-1}. If the arterial pressure could not be lowered, nitroglycerine infusion at a rate 1–5 μg kg^{-1} min^{-1}, and repeated boluses of propranolol 100 μg (up to 50 μg kg^{-1}) were injected. If the systolic arterial pressure was not above 100 mm Hg, none of the hypotensive agents were administered.

Table 1 Definition of quality of the wake-up test

Scale	Definition
Good	Quiet awakening, patient obeys orders, voluntary movements of hands and feet
Satisfactory	Sudden awakening, patient seems confused, spontaneous movement of extremities not endangering spondylodesis
Poor	Dramatic awakening, patient is agitated, violent trunk movements threatening stability of the device

The wake-up test consisted of lightening anaesthesia until the patients were able to move hands and feet upon command, and was performed as follows; the surgeon informed the anaesthetist around 20 min before device insertion to prepare for a wake-up test. During this period no atracurium was injected, to achieve a desirable twitch response (four twitches). After the surgeon's request for wake-up test, infusion pumps were stopped, the anaesthesia ventilator disconnected, and the lungs manually ventilated. After spontaneous ventilation was started, and no residual neuromuscular block was detected, the patient's name was repeated every 30 s followed by the request to open and close fingers of hand. When the patients moved their fingers, they were asked to move both feet. When the patients did not respond to command within 20 min from discontinuation of anaesthesia, naloxone 0.2 mg was injected i.v. every minute until the patients responded. Times was measured from the discontinuation of anaesthesia until start of spontaneous ventilation (T_1) and from then until responding to command (T_2). Quality of the wake-up test was evaluated on a 3-point rank scale (Table 1).

When the wake-up test was completed, for each kilogram of body weight, i.v. boluses of midazolam 30 μg, lidocaine 1 mg, atracurium 0.4 mg in both groups, and alfentanil 20 μg (in PA group) or remifentanil 1 μg (in PR group) were injected. Infusion pumps were restarted in each group. The lungs were ventilated again and maintenance of anaesthesia was continued in each group as before. Patient characteristics, wake-up times, and quality of arousal were recorded.

Statistical analysis was performed using SPSS 12 for Windows. Data are expressed as means (SD). Continuous variables (age, weight, duration of operation and anaesthesia, and wake-up times), were analysed using Student's *t*-test, or Mann–Whitney *U*-test, depending on distribution or significant differences in variances. The frequency distributions (sex and quality of the wake-up test) were subjected to χ^2-test. *P*-value <0.05 was considered statistically significant.

Results

Sixty patients (30 in each group) were enrolled in this study. Both groups had similar characteristics for age, weight and duration of anaesthesia and surgery (Table 2). Wake-up time

Table 2 Patient and surgical characteristics. Data are expressed as mean (SD or range) unless otherwise noted. PA, alfentanil; PR, remifentanil group. *Not significant

	PA	PR
Sex (male/female)*	14/16	12/18
Age (yr)*	21 (14–28)	19 (16–24)
Weight (kg)*	50 (9)	49 (6)
Duration of surgery (min)*	230 (24)	225 (18)
Duration of anaesthesia (min)*	256 (35)	242 (28)

Table 3 Wake-up time [mean (SD)]. T_1, time from discontinuation of anaesthesia until start of spontaneous ventilation; T_2, time from end of T_1 until response to command. *$P<0.01$

	PA	PR
T_1 (min)*	6.1 (4)	3.6 (2.5)
T_2 (min)*	7.5 (4.5)	4.1 (2)

Table 4 Quality of wake-up test. *Not significant

	PA (*n*)	PR (*n*)
Good*	25	27
Satisfactory*	5	3
Poor*	–	–

(T_1 and T_2) was significantly shorter in remifentanil (PR) group [3.6 (2.5) and 4.1 (2) min] than alfentanil (PA) group [6.1 (4) and 7.5 (4.5) min] ($P<0.01$) (Table 3). In contrast, the quality of wake-up test was not significantly better in PR than PA group (Table 4).

Discussion

The study evaluated the wake-up time between two TIVA protocols in patients undergoing PSF.

Shorter wake-up times were found in the PR than the PA group. Although, we did not reach statistically significant differences in the quality of wake-up test between the two groups, the significantly shorter wake-up time in the PR group observed in this study imparts significance as obtaining a shorter wake-up time in itself remains an important goal for the anaesthetist. In our previous study, wake-up time was found to be shorter during PA anaesthesia compared with midazolam–alfentanil anaesthesia (F. Imani, A. Jafarian, V. Hassani and E. Ameri, unpublished observation).

As mentioned above, spinal cord damage is one of the serious but rare complications resulting from vascular compression.[15] Major causes include an overstretching of the spinal arteries and an accidental surgical trauma to the spinal cord; acute, prolonged marked hypotension, or both, and compression of the spinal cord as a result of haematoma formation.

Neurological methods and wake-up test are often used to detect intra-operative compromise of the spinal cord function. Neurological methods include the application of somatosensory evoked potentials (SSEPs) and motor evoked potentials (MEPs). Changes in wave patterns reveal a possible damage to the spinal cord. However, SSEP only monitors signal conduction in the sensory columns of the spinal cord. These tracts are concentrated posterio-medially and thus away from the anterior aspect of the spinal cord, where the vascular insult generally occurs. Moreover, as changes in the anterior horn cells may result in changes in the SSEP, a spinal cord injury may be missed with this technique. Furthermore, volatile anaesthetic agents produce a dose-related reduction in the amplitude and increases in the latency of the cortical component of the SSEP, especially when N_2O is used. These changes are most pronounced with enflurane and least with halothane.[16] MEP may be considered as an alternative to SSEP during spinal procedures. For greater security, combined SSEP and MEP is advocated, although more experience is required to confirm whether iatrogenic defects detected by the latter are sufficiently reversible to prevent persistent neurological compromise.[17] However, most procedures eliciting MEP during operation are highly sensitive to anaesthesia, particularly volatile anaesthetic agents.[18] Also, neuromuscular blocking drugs greatly reduce the MEP recorded from muscle.[19] On the other hand, hypotension, hypothermia and haemodilution also influence successful evoked potentials data.[4] Therefore, the intra-operative wake-up test is still considered to be the 'gold standard' and consists of patient awakening with observation of voluntary limb movement. This method helps to detect early spinal cord dysfunction which may be reversible by reducing the vertebral distraction or by removing the rods.[3 5 6] This test was initially described by Vauzelle and colleagues[7] in 1973, and has proved to be valuable in young patients with nonparalytic scoliosis.

Certain hazards of the wake-up test do exist. These include recall, pain, emotional damage, accidental tracheal extubation, air embolism via exposed epidural veins, and rod dislocation or fracture during coughing. For these reasons, at the time of awakening, the patient should be calm and painless, be conscious enough to obey order, and have amnesia for the event. However, these hazards have not complicated the reported series.[5 6]

Retarded patients, infants and young children are not good candidates for a wake-up test and might benefit from SSEP or MEP during surgery. Paraplegic patients also are not good candidates for either wake-up test or SSEP, but certainly need intra-operative sensory and motor monitoring to prevent extension of existing neurological deficits.

Evoked potentials are routinely used in some spine centres and the wake-up test in others. Both methods may be used concomitantly, but multiple wake-up tests are strongly recommended when evoked potential data

cannot be obtained.[4] Also, neither of them is infallible, and neurological deficits (such as paraplegia or quadriplegia) have been reported both after normal SSEP[17 20–22] and after a normal wake-up test.[23]

Wake-up test requires the use of an anaesthetic technique which allows rapid awakening to a level of consciousness where a response to commands can be accomplished. Compared with old long acting opioids, rapid and ultra-rapid opioids can have an important place for this aim.[14] However, continuous infusion of short-acting hypnotics (such as propofol) is also of great value when compared with old volatile anaesthetics such as halothane or isoflurane.[24] Although, in a recent study the new volatile anaesthetic desflurane had a shorter wake-up time compared with propofol, evoked potential data were difficult to obtain.[25]

Although mild to moderate deliberate hypotension has been widely used in spinal surgery to reduce blood loss and to facilitate a bloodless field; acute, prolonged hypotension, or both may jeopardize spinal cord vascularization, and mean arterial pressures should be maintained between 65 and 70 mm Hg during surgery.[4] Unchecked and persistent hypotension may lead to inadequate perfusion of the spinal cord, resulting in spinal cord dysfunction that may be noted by acutely evoked potential data loss, even before any instrumentation.[26]

In conclusion, in our study, we observed that wake-up time was shorter in PR than in the PA infusion.

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